American Journal of Medical Genetics 68:367–368 (1997)

Letter to the Editor

Brachmann-de Lange Syndrome

To the Editor:

We read with interest the report of Manouvrier et al. [Am J Med Genet 62:268–273, 1996] in a recent issue of the journal on the diagnosis of Brachmann-de Lange (BDLS) syndrome by prenatal ultrasound examination. We had a similar experience in our institution. A 19-year-old woman of 20 weeks of gestation underwent a routine ultrasound examination that disclosed a large diaphragmatic hernia. The fetus also was growth retarded with micromelia and microbrachycephaly. The face showed a small bulging nose, long bulging philtrum and micrognathia (Fig. 1). Based on the association of IUGR, limb anomalies, and characteristic face, the obstetrician diagnosed BDLS. The woman delivered a male infant at 36 weeks of gestation who died shortly after birth from severe pulmonary hypoplasia. Autopsy findings confirmed the prenatal diagnosis. The infant showed the typical BDLS face (Fig. 2) and phenotype. He also had a large bilateral diaphragmatic hernia, which is not commonly a part of the syndrome but has been reported [Kousseff, 1994]. Unfortunately, as in the three cases reported by Manouvrier et al., we did not save maternal serum or placental tissue to confirm the absence of pregnancy-associated plasma protein A (PAPPA).

Children born with BDLS have significant morbidity and mortality. Presently, there is no consistent genetic abnormality or biomarker for this syndrome and its diagnosis is based exclusively on the morphologic description of its phenotype. Chromosome 9 abnormalities have been implicated as possible causes because of the association with affected children and PAPPA [Opitz, 1994]. PAPPA has been reported absent in the maternal serum and placental tissue of affected infants, and PAPPA maps to chromosome 9.

Based on our findings and those of the authors, it seems likely that in the future the prenatal diagnosis of BDLS will be made with greater certainty. It is possible by ultrasound examination to demonstrate the characteristic facies and associated anomalies. Once the diagnosis is made or strongly suspected, the attending physician should obtain maternal serum and fresh placental tissue at the time of delivery to determine the level of PAPPA. If PAPPA is consistently absent in

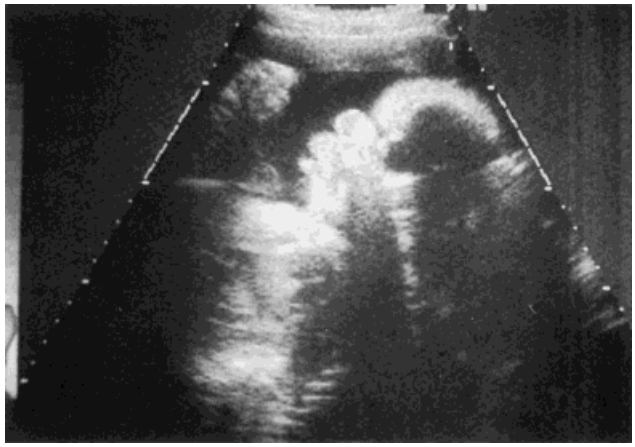

Fig. 1. Ultrasound examination of a 20-week fetus showing bulging nose, long philtrum, and micrognathia.

Fig. 2. The corresponding BDLS facies in autopsied infant, born at 36 weeks of gestation.

*Correspondence to: Dr. Jeanne Ackerman, University of South Florida, Department of Pathology, Davis Island, P.O. Box 1289, Tampa, FL 33601.

Received 19 April 1996; Accepted 19 April 1996

BDLS infants and their mothers, then together with a complete prenatal ultrasound, this finding may provide a reliable diagnostic test. We believe that the role of PAPPA and its association with chromosome 9 remains an enigma that needs further investigation. Prenatal suspicion or diagnosis by ultrasound will expedite this process.

REFERENCES

Kousseff BJ, Newkirk P, Root AW (1994): Brachmann-de Lange Syndrome, 1994 Update. Arch Pediatr Adolesc Med 148:749–755.

Manouvrier S, Espinasse M, Vaast P, Boute O, Farre I, Dupont F, Puech F, Gosselin B, Farriaux J-P (1996): Brachmann-de Lange Syndrome: Pre- and Postnatal Findings. Am J Med Genet 62: 268–273.

Opitz JM (1994): Brachmann-de Lange Syndrome: A continuing enigma. Arch Pediatr Adolesc Med 148:1206–1208.

Jeanne Ackerman*
Enid Gilbert-Barness
Department of Pathology
University of South Florida
Tampa, Florida